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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HENRY, MICHAEL C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,329	BISSERY, MARIE CHRISTINE	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 12/03/03.

The amendment filed 12/03/03 affects the application, 09/809,329 as follows:

1. Claims 1,2,11,13 have been amended.
2. Applicant responds to the 102 and 103 rejections by amending claims 1,2,11,13.
3. Pending claims are claims 1-20.

The responsive to applicants' arguments is contained herein below.

Claim Objections

Claims 2 and 9-11 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 2 and 9-11 recite the intended use of the composition. However, these claims are composition claims and the recitation of the intended use of the composition is not a further limitation of the claim. In particular, the recitation of an intended use to treat a specific cancer or tumor, must result in a tangible structural difference between the product of the independent claim and the product set forth in the dependent claim. In the absence of said structural difference between the product of the independent claim and that of the said dependent claim, said dependent claim is seen to be a substantial duplicate, and said recitation is not afforded critical weight and fails to further limit the product of said dependent claim. The examiner gives very little weight to said intended utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10,13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The terms "camptothecin derivative" renders the claims indefinite. More specifically, in the absence of the specific derivatizations to the chemical core claimed (CCC) or distinct language to describe the structural modifications or the chemical names of the derivatized (CCC) of this invention, the identity of said derivatives would be difficult to describe and the metes and bounds of said derivatives that applicant regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims. Therefore, the identity of this composition component is indefinite. Furthermore, the term " camptothecin derivative " in all occurrences is seen to be indefinite where applicant fails to provide how the core compound is modified to obtain some derivatized version which is intended to be an integral part of the composition claimed.

The term "topoisomerase II inhibitor" in claims 1,2,3,6,13,14,17, renders the claims indefinite. This term is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. More specifically, it is unclear which substance (s) constitutes a topoisomerase II inhibitor, especially in the absence of any indicated name, structure and/or form.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Furuta et al. (Jpn J Cancer Chemother 18 (3): 393-402, 1991).

In claim 1, applicant claims "a therapeutic synergistic pharmaceutical composition for solid tumors comprising an effective amount of camptothecin, or a camptothecin derivative, in combination with an effective amount of a topoisomerase II inhibitor, wherein said composition provides a therapeutic synergistic effect in the treatment of solid tumors."

Furuta et al. disclose applicant's claimed, therapeutic synergistic pharmaceutical composition, comprising an effective amount of camptothecin derivative (CPT-II), in combination with an effective amount of a topoisomerase II inhibitor (adriamycin or doxorubicin), wherein said composition provides a therapeutic synergistic effect in the treatment of tumors (see summary or abstract and tables). The applicant's composition of claims 2-4,6,7, 9-12, which are drawn to specific topoisomerase II inhibitors, camptothecin or camptothecin derivatives and said composition for treating specific tumors, is also anticipated by Furuta et al. (see summary or abstract and tables). It should be noted that claims 2 and 9-11 are composition claims and the recitation of the intended use of the composition is not a further limitation of the claim. In particular, the recitation of an intended use to treat a specific cancer or tumor, must result in a tangible structural difference between the product of the independent claim and the product set forth in the dependent claim. In the absence of said structural difference between the product of the independent claim and that of the said dependent claim, said dependent claim is seen to be a substantial duplicate, and said recitation is not afforded critical weight and fails to further limit the product of said dependent claim. The examiner gives very little weight to said intended utility.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5,8 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuta et al.

In claims 5 and 8, applicant claims a composition as in claim 3 and 6 respectively, wherein said antibiotic is daunomycin (claim 5) and wherein said epipodophyllotoxin is teniposide (claim 8).

Furuta et al. disclose a composition as in claims 3 and 6 respectively, wherein said antibiotic is adriamycin and wherein said epipodophyllotoxin is etoposide.

The difference between applicant's claimed composition and the composition taught by Furuta et al. is that the applicant's antibiotic is daunomycin as compared to adriamycin and applicant's epipdophyllotoxin is teniposide as compared to etoposide. However, daunomycin and adriamycin are both well known anthracycline antibiotics or antitumor agents of very similar structure. That is, they can be considered species of the same genus and are expected to share chemical properties. Also, the epipdophyllotoxin, teniposide and etoposide are antitumor agents that can also be considered species of the same genus and are expected to share chemical properties.

It would have been obvious to one having ordinary skill in this art, at the time the claimed invention was made, in view of Furuta et al., to prepare and administer a therapeutic pharmaceutical composition, comprising an effective amount of camptothecin, or a camptothecin

derivative, in combination with an effective amount of a topoisomerase II inhibitor like daunomycin (which can be considered to belong to the same genus as adriamycin (doxorubicin), for the treatment of different tumors.

One having ordinary skill in the art would have been motivated in view of Furuta et al., to prepare and administer a therapeutic pharmaceutical composition, comprising an effective amount of camptothecin, or a camptothecin derivative, in combination with an effective amount of a topoisomerase II inhibitor like daunomycin based on need, like the type and/or degree of severity of the tumor.

In claim 13, applicant claims a method of treating a solid tumor, comprising administering an effective amount of camptothecin, or a camptothecin derivative, as a first agent, in combination with an effective amount of a topoisomerase II inhibitor as a second agent, wherein the agents are administered simultaneously, semi-simultaneously, or separately, and wherein said first and second agents provide a therapeutic synergistic effect in the treatment of said solid tumor. Dependent claims 14-19 are drawn to methods involving specific camptothecin derivatives (teniposide and etoposide) and specific topoisomerase II inhibitors (adriamycin (doxorubicin) and daunomycin (daunorubicin)). It should be noted that claims 14-19 are also obvious in view of Furuta et al., since Furuta et al. also use the same antitumor agents (adriamycin and etoposide) or antitumor agents that belong to the same genus as (daunomycin) and (teniposide). Dependent claim 20 is drawn to the method according to any one of claims 13-19, wherein the camptothecin derivative is administered orally.

Furuta et al. disclose a method of treating a tumor (L 1210 leukemia), comprising administering an effective amount of a camptothecin derivative, as a first agent, in combination with administration of an effective amount of a topoisomerase II inhibitor as a second agent,

wherein the agents are administered simultaneously, semi-simultaneously, or separately and wherein said first and second agents provide a synergistic effect (see abstract and tables).

The difference between applicant's claimed method and the method taught by Furuta et al. is the type of tumor that is treated and the form of administration of said agents.

It would have been obvious to one having ordinary skill in this art, at the time the claimed invention was made, in view of Furuta et al., to use the method of Furuta et al. to treat various types of tumors like solid tumors, and to use antitumor agents taught by Furuta et al. that belong to the same genus as (adriamycin and daunomycin) and (teniposide and etoposide) for the treatment of different tumors using any common administrative form (e.g. oral administration), based on need, like the type and/or degree of severity of the tumor and the subject that is treated.

One having ordinary skill in the art would have been motivated in view of Furuta et al., to use the method of Furuta et al. to treat various types of tumors like solid tumors, and to use antitumor agents taught by Furuta et al. that belong to the same genus as (adriamycin and daunomycin) and (teniposide and etoposide) for the treatment of different tumors using any common administrative form (e.g. oral administration), based on need, like the type and/or degree of severity of the tumor and the subject that is treated.

Response to Amendment

Applicant's arguments filed December 3, 2003 have been fully considered but they are not persuasive.

The applicant argues that applicant has overcome the heavy presumption that the term "synergy" should be given its ordinary and customary meaning, because applicant has acted as her own lexicographer. Applicant also acknowledges that

First, the claim term will not receive its ordinary meaning if patentee acted as his own lexicographer and clearly set forh a definition of the disputted claim term in either the specification or prosecution history. Second, a claim term will not carry its ordinary meaning if the intrinsic evidence show that the patentee distinguised that term from prior art.

However, applicant has not **clearly** set forth a definition of the disputed claim term, synergy(or synergistic or synergism). Particularly, applicant set forth a definition for "therapeutic synergy" by stating in the specification that a combination manifests therapeutic synergy if it is therapeutically superior to one or other of the constituents used at its optimum dose (T.H. Corbett et al., *Cancer Treatment Reports*, **66**:1187 (1982)). Furthermore, in the claims applicant claims a synergistic therapeutic pharmaceutical composition, but therapeutic synergy as defined by applicant is not identical to the synergistic therapeutic pharmaceutical composition claimed by applicant. Synergistic therapeutic pharmaceutical composition, implies a therapeutic pharmaceutical composition that exhibits synergy (or a synergistic effect) in general, regardless of whether the synergy is therapeutic synergy as defined by applicant. Also, the applicant has not set forth a definition for the claimed term synergistic therapeutic pharmaceutical composition which is not identical to therapeutic synergy and thus applicant has not distinguised said term from the prior art. Consequently, by claiming a synergistic therapeutic pharmaceutical composition, applicant has claimed Furuta's therapeutic pharmaceutical composition which is synergistic. It should also be noted that not all of the claims use the word therapeutic with synergistic or synergy (see claim 13 which recites … a synergistic effect …). Moreover, the specification defines the term "therapeutic synergy" whereas the applicant claims synergy in general, (as in synergistic therapeutic pharmaceutical composition (claims 1,2 and 11) and synergistic effect (claim 13)), and thus does not define the term, synergy (or synergistic)

with reasonable clarity, deliberateness, and precision necessary for departure from ordinary meaning. For example, in Abbott Laboratories v. Syntron Bioresearch Inc., 67 USPQ2d 1337 (CA FC 2003), the

"Term "analyte," as used in claims of patent for chemical analysis apparatus and method, should be given plain meaning adopted by federal district court, namely, "the substance that the test is designed to detect if present in the liquid being tested," even though patentee defined "analyte" in specification, since specification provides two alternative definitions for term, and thus does not define term with reasonable clarity, deliberateness, and precision necessary for departure from ordinary meaning." See Abbott Laboratories v. Syntron Bioresearch Inc., 67 USPQ2d 1337 (CA FC 2003).

Consequently, because applicant fails to define the term with reasonable clarity, deliberateness, and precision necessary for departure from ordinary meaning, the definition of synergism (or synergistic effects or synergy) is not limited to the applicant's condition or term that he/she refers to as optimum dose (i.e., highest non-toxic dose). Some ordinary meaning or definitions includes a definition from Webster's New World Dictionary (3rd college edition, 1988, page 1358) which defines synergism as "the simultaneous action of separate agencies which, together, have greater total effect than the sum of their individual effects; said esp. of drugs ...." Yet another definition states that "it is not uncommon for the effect of two chemicals on an organism to be greater than the effect of each chemical individually, or the sum of the individual effects. The presence of one chemical enhances the effects of the second. This is called a synergistic effect or synergy, and the chemicals are sometimes described as showing synergism." (see, http://physchem.ox.ac.uk/MSDS/glossary/synergistic_effect.html, The Physical and Theoretical Chemistry Laboratory,Oxford University, England Chemical Safety Information - Glossary). Thus, synergism is not limited to an optimum dose (i.e., highest non-toxic dose) and therefore, Furuta et al. do not have to disclose an optimum dose (i.e., highest

non-toxic dose) in reporting synergism or synergistic effects of their composition. Also, Furuta et al. data of Table 3 shows that the effect (survival times) of two chemicals (CPT-II and adriamycin) on the inoculated mice (an organism) is greater than the effect of each of these chemicals individually (for example, 12.5 mg/kg of CPT-II + 6.25 mg/kg of adriamycin produces a survival time of 16.5 ± 1.7 days whereas, 12.5 mg/kg of CPT-II produces a survival time of 10.8 ± 0.4 days and 6.25 mg/kg of adriamycin produces a survival time of 11.7 ± 0.7 days; based on three administrations (days 1,5,9) per dosing regimen). This result complies with the latter stated definition of synergism or synergistic effect and also with applicant's definition excluding the limitation or term, "when used at maximum dose". In addition, applicant argues that the Examiner's statement pertaining to the data in table 3, is not supported by all, and is contrary to some, of the data in Furuta. However, the aforementioned results of Furuta et al. are the results of a single experiment at the given concentrations and a comparison to other results from other experiments (as presented or argued by applicant) is irrelevant, especially since other experiments involve different conditions. Furthermore, applicant argues that the rate of survival for mice treated with the therapeutic synergistic combination is almost double the rate of survival for the mice treated with the individual constituents alone, and more than three times the rate reported in Furuta. However, in the absence of a side-by-side comparison between applicant's composition and Furuta et al. composition (which involves the same specific conditions and experimental parameters) one cannot assume that Furuta et al. composition would not give the same results. As applicant indicated, the data in Table IV (i.e., applicant's data) is not directed to days of survival as in Furuta, but instead, it is directed to the time in days for the tumors to reach 1000 mg. This difference in measured parameters or conditions is one example that indicates the absence of the said side-by-side comparison. Moreover, applicant's therapeutic synergistic

pharmaceutical composition, as claimed reads on Furuta et al.'s composition, since Furuta et al. composition contains the same ingredients or components as applicant's composition. It should be noted that applicant does not claim any specific amounts, quantities or concentrations of the said composition or components of the composition that equates to a maximum or optimum dose, or that renders his/her composition different from Furuta et al.'s composition. Thus, Furuta et al's composition is the same as applicant's claimed composition and should have the same therapeutic synergistic effect when administered under the same conditions.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8:30 am to 5:00 pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-1235.

MCH

April 28, 2004.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600